

## REMARKS

### **I. Status of the claims**

Claims 93-143 are pending. Claims 1-25, 84, and 86-92, were previously canceled without prejudice or disclaimer. Claims 26-83 and 85 are withdrawn from consideration. Of course, Applicants reserve the right to file one or more continuing applications to the cancelled subject matter. Claims 93, 99, 100, 102, 103, 113, 117, and 127 have been amended for the reasons that follow below.

Claims 140-143 have been added and are directed to a chromosome vector that comprises (i) a chromosome fragment that contains the human chromosome #21 centromere, (ii) two telomere sequences, (iii) at least one recognition sequence for a site-directed recombination enzyme, and (iv) a marker gene. The new claims are fully supported by the specification at, for instance, page 65, line 24 to page 67, line 2. There, Applicants describe the use of the SC20 chromosomal fragment as a chromosomal "vector" (page 65, lines 27-28), and similarly that a human chromosome 21 fragment can also be used as a vector (page 66, last two lines to page 67, first line). Applicants also disclose that the loxP nucleotide sequence can be inserted into the SC20 fragment (page 66, lines 5-10). Accordingly, these claims do not introduce any new matter and Applicants respectfully request that claims 140-143 be entered.

### **II. Summary of the Office Action**

(i) Claims 93 and 113 are rejected under 35 U.S.C. § 112, second paragraph because "it is unclear if the two chromosome fragments in the claim are adjacently located in the recombinant chromosome." Office Action dated July 2, 2003, at page 3.

(ii) Claims 99, 100, and 102 are rejected under 35 U.S.C. § 112, second paragraph because "it is unclear which fragment corresponds to which gene locus." Office Action at page 3.

(iii) Claims 117 and 127 are rejected under 35 U.S.C. § 112, second paragraph because "the claim language does not state that the cells are isolated." Office Action at page 3.

**III. Applicants' amendment overcomes the Examiner's rejections under 35 U.S.C. § 112, second paragraph**

**(i) *The chromosome fragments of claims 93 and 113 may or may not be "adjacently located" in the recombinant chromosome***

The Examiner rejected claims 93 and 113 under 35 U.S.C. § 112, second paragraph alleging that "it is unclear if the two chromosome fragments in the claim are adjacently located in the recombinant chromosome." Office Action dated July 2, 2003, at page 3.

The term "*not adjacently located in a natural chromosome*" is intended to distinguish (A) the presently claimed recombinant chromosome, into which a recombinase recognition site is present between *distinct* chromosomal fragments, as a consequence of recombination, from (B) a single, naturally-occurring chromosome, or fragment thereof, into which a recombinase site has been introduced. In the latter case, when a recombinase site, such as a loxP site, is inserted into the chromosome fragment, the fragment appears as though it is "divided" or "split" into two chromosomal fragments. According, these fragments *had been* adjacently located prior to the insertion of the loxP sequence. By contrast, the distinct chromosome fragments of the presently claimed recombinant chromosome, *e.g.*, the SC20 fragment, *had not been* adjacently located. The amended claims clarify this positional arrangement.

Accordingly, there is no question of clarity with respect to any arrangement of such elements in the recombinant chromosome and Applicants respectfully request that the Examiner withdraw this rejection.

**(ii) *Claims 99, 100, 102, and 103 have been amended to clarify which fragment corresponds to which gene locus***

The Examiner rejected claims 99, 100, and 102 alleging that "it is unclear which fragment corresponds to which gene locus." Office Action at page 3.

Applicants have amended claims 99, 100, 102, and 103 to recite which chromosomal fragment comprises which antibody gene. Thus, claims 99 and 100 clarify that the chromosome #14 fragment of claim 98 comprises the human antibody heavy-chain gene locus and that the chromosome #2 fragment of claim 98 comprises the human antibody light-chain kappa gene locus. Similarly,

claims 102 and 103 clarify that the chromosome #14 fragment of claim 101 comprises the human antibody heavy-chain gene locus and that chromosome #22 fragment of claim 101 comprises the human antibody light-chain lambda gene locus. Accordingly, claims 99, 100, 102, and 103 are free from objection and, therefore, the rejection is moot.

(iii) *Claims 117 and 127 have been amended to clarify  
that the first and second cells are "isolated"*

The Examiner rejected claims 117 and 127 under 35 U.S.C. § 112, second paragraph because "the claim language does not state that the cells are isolated." Office Action at page 3. Applicants have amended claims 117 and 127 to recite that the "first" and "second" cells are "isolated." Accordingly, Applicants respectfully request that the Examiner withdraw this rejection.

IV. Conclusion

In view of the above remarks and amendments, it is respectfully submitted that this application is in condition for allowance. Early notice to that effect is earnestly solicited. The Examiner is invited to telephone the undersigned at the number listed below if the Examiner believes such would be helpful in advancing the application to issue.

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